

## REMARKS

The Office Action presents the following points: 1) the specification is objected to for the reason that the title is considered not descriptive and further because the brief description of the drawings fails to refer to parts F-H of FIG. 5; 2) claim 29 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite; 3) claims 1-3, 13-16 and 29 stand rejected under 35 U.S.C. §112, first paragraph, for lack of enablement; 4) claims 1-3, 6, 13, 14 and 16 stand rejected under 35 U.S.C. §102(b) as anticipated by WO 00/56879 (Weber et al.); 5) claims 1, 3-6, 13 and 29 stand rejected under 35 U.S.C. §102(b) as anticipated by De Robertis et al. (US 5,679,783); and 6) claim 15 stands rejected under 35 U.S.C. §103(a) as unpatentable over Weber in view of Hunter et al. (US5,716,981).

In response, Applicant presents amended claims 1, 4, 14 and 29, cancels claims 3 and 6, and amends the title and specification herein.

In view of the amendments and remarks presented herein, Applicant respectfully requests reconsideration and withdrawal of the objections and rejections presented in the Office Action.

### 1. Specification

Applicant has amended herein the title to this application and also the brief description of the drawings in connection with FIG. 5 to refer to parts F-H. Applicant respectfully submits that these amendments traverse the objection to the specification.

### 2. 35 U.S.C. §112, second paragraph

Applicant has amended claim 29 in connection with its reference to SEQ ID NO:1. Applicant respectfully submits that the amendment to claim 29 traverses its rejection as being indefinite under §112, second paragraph.

### 3. 35 U.S.C. §112, first paragraph

Applicant has amended independent claims 1 and 14 to incorporate the feature of claim 6 wherein the bone morphogenic protein is bone morphogenic protein-4 and accordingly canceled claim 6. Applicant respectfully submits that the amendments to these claims traverse the rejection of claims 1-3, 13-16 and 29 under 35 U.S.C. §112, first paragraph, for not reasonably providing enablement of the claimed invention wherein the

active agent inhibits bone morphogenic proteins other than bone morphogenic protein-4.

4. 35 U.S.C. §102

Claims 1-3, 6, 13, 14 and 16 stand rejected as anticipated by Weber et al. (WO 00/56879). Applicant respectfully traverses this rejection.

Weber is directed to heterotopic ossification (HO) that is a normal bone formation at ectopic sites like muscle and connective tissue and also orthotopic ossification as characterized by normal bone formation contiguous with the normal skeleton. More particularly, Weber et al. disclose use of a bone morphogenic protein antagonist to treat bone disease heterotopic ossification (HO) where bone like structures are formed in wrong places such as in muscles and joints causing decreased motion and severe pains. The specific antagonists taught by Weber are cytokines, and not polypeptides or more specifically a modified bone morphogenic polypeptide or a prodrug thereof. (See, e.g., page 1, lines 15-32 and page 6, lines 15-18.)

Weber et al. fail to address the problem addressed by Applicant, namely vascular inflammation, and fail to present any solution to vascular inflammation. Further, Weber et al. fail to disclose any type of compound for inhibiting or reducing vascular inflammation by interfering with binding of bone morphogenic protein or a fragment thereof to a bone morphogenic protein receptor, as recited in independent claims 1 and 14. Further, Weber et al. fail to teach or suggest wherein the bone morphogenic protein receptors are vascular cell bone morphogenic protein receptors as recited in claims 1 and 14. Weber et al. yet further fail to teach or disclose wherein the bone morphogenic protein antagonist or prodrug thereof or the bone morphogenic protein receptor antagonist or prodrug thereof comprises a modified bone morphogenic polypeptide or prodrug thereof as recited in claims 1 and 14.

Applicant notes the statement at pages 6-7 of the Office Action acknowledging that "Weber et al. do not explicitly state that the receptors are vascular cell bone morphogenic protein receptors." The Office Action further states, however, "the receptors taught by Weber et al. are inherently vascular cell bone morphogenic protein receptors." Applicant respectfully challenges this bald statement which is presented without any support, particularly in view of Weber et al.'s teaching only of an antagonist to inhibit heterotopic ossification and/or orthotopic ossification in places such as muscles and joints.

In view of the foregoing, Applicant respectfully submits that Weber et al. fail to

anticipate independent claims 1 and 14.

Applicant further respectfully submits that Weber et al. fail to anticipate claim 2. The Office Action acknowledges that Weber et al. did not explicitly state that the receptors are vascular cell bone morphogenic protein receptors. Accordingly, Weber et al. fail to disclose a bone morphogenic protein antagonist that comprises a modified bone morphogenic polypeptide or a prodrug thereof "in an amount sufficient for inhibiting vascular inflammation by competitively inhibiting binding of bone morphogenic protein to endothelial bone morphogenic protein receptors, wherein binding of said modified bone morphogenic protein to said bone morphogenic protein receptor does not activate said receptor" and wherein as recited in claim 1 "the bone morphogenic protein receptor is a vascular cell bone morphogenic protein receptor."

Claims 13 and 16 being dependent upon claims 1 and 14, respectively, are likewise not anticipated by Weber et al. for the reasons stated above in connection with their base independent claims 1 and 14.

Claims 1, 3-6, 13 and 29 stand rejected as anticipated by De Robertis et al. (US 5,679,783). Applicant respectfully traverses this rejection.

De Robertis et al., like Weber et al., fail to address the problem addressed by Applicant, namely vascular inflammation, and fail to present any solution to vascular inflammation. Further, De Robertis et al. fail to disclose any type of compound for inhibiting or reducing vascular inflammation by interfering with binding of bone morphogenic protein or a fragment thereof to a bone morphogenic protein receptor, as recited in independent claims 1 and 14. Further, De Robertis et al. fail to teach or suggest wherein the bone morphogenic protein receptors are vascular cell bone morphogenic protein receptors as recited in claims 1 and 14. De Robertis et al. yet further fail to teach or disclose wherein the bone morphogenic protein antagonist or prodrug thereof for the bone morphogenic protein receptor antagonist or prodrug thereof comprises a modified bone morphogenic polypeptide or prodrug thereof, as recited in claims 1 and 14.

Applicant notes the statement at pages 7-8 of the Office Action acknowledging that "De Robertis et al. do not explicitly state that the receptors are vascular cell bone morphogenic protein receptors." The Office Action further states, however, "the receptors taught by De Robertis et al. are inherently vascular cell bone morphogenic receptors." Applicant again respectfully challenges this bald statement which is presented without any

support, particularly in view of De Robertis et al.'s teaching that their invention is generally related to growth factors, neurotropic factors, and their inhibitors, and more particularly to a "growth factor with dorsal growth (and neural tissue) inducing activity." (Col. 1, lines 10-14). Instead, De Robertis et al. is basically directed to a disclosure of chordin *per se*. In this regard, Applicant notes that De Robertis et al. is not applied against pending claim 2 of the present application.

With respect to claim 5, Applicant respectfully further submits that De Robertis et al. fail to disclose a composition wherein the bone morphogenic protein antagonists "consists of " "the N-terminal fragment of noggin, chordin, DAN or veinless," and that no citation is presented in the Office Action showing where De Robertis et al. anticipate claim 5.

In view of the foregoing, Applicant respectfully submits that claims 1, 3-6, 13 and 29 are not anticipated by De Robertis et al.

#### 5. 35 U.S.C. §103

Claim 15 stands rejected under 35 U.S.C. §103. Applicant respectfully submits that claim 15, being dependent upon claim 14, is allowable for the same reasons as claim 14 as described above.

#### 6. New Claims

New Claims 30-33 are added. These claims are either directly or indirectly dependent upon independent claim 1 and are believed allowable for the same reasons as independent claim 1 stated above. Further, Applicant respectfully submits that new claims 30-33 are allowable independent of the reasons for claim 1, for the reason that none of the cited references teach or suggest the features cited therein.

Support for claims 30 and 31 is found in the substitute specification at page 11, lines 23-30, and support for claim 32 and 33 is found in the substitute specification at page 10, lines 27-34.

**CONCLUSION**

In light of the foregoing remarks set forth above, Applicants respectfully submit that the present application is in condition for allowance and as such, favorable allowance of the present application is hereby courteously requested. If, in the opinion of the Examiner, a telephone conference would expedite the examination of this matter, the Examiner is invited to call the undersigned attorney at (770) 933-9500.

Respectfully Submitted,

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